

Claim 32 has been canceled.

**REMARKS UNDER 37 CFR § 1.111**

**Formal Matters**

Claims 1-11, 13, 18-26 and 28-32 were examined. Claims 1-11, 13, 18-26 and 28-32 were rejected.

Claims 1-5, 8-11, 13 and 20-25 are pending after entry of the amendments set forth herein. Claims 6-7, 12, 14-19 and 26-32 are canceled.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached is captioned "Version with markings to show changes made."

Applicants respectfully request reconsideration of the application in view of the amendments and remarks made herein.

Support for the amendments to claims 1-5 and 8-11 can be found throughout the specification, at, for example, page 3, line 14, page 6, lines 19 and 22-24, page 11, line 19 through page 15, line 28. Support for the amendments to claims 13 and 20-25 can be found throughout the specification, at, for example, page 3, line 14, page 6, lines 19 and 22-24, page 14, lines 14-20 and page 51, line 10 though page 53, line 16. As such, no new matter has been added.

**Rejection under 35 U.S.C. § 112, 1<sup>st</sup> paragraph (enablement).**

Claims 5-11, 13, 18-26 and 28-32 have been rejected under 35 U.S.C. § 112, 1<sup>st</sup> paragraph for assertedly being non-enabling. Claims 6-7, 12, 14-19 and 26-32 are canceled.

Claims 5, 8 and 10 have been rejected for assertedly being non-enabling because the "disrupted gene need not comprise the sequence set forth as SEQ ID NO: 1." (Office Action dated January 14, 2003, page 3) The Office Action asserted that "the specification is enabling for a homozygous knockout mouse comprising a disruption in the stefin homolog gene set forth in SEQ ID NO: 1 and exhibiting phenotypic features . . . as compared to wild-type mice." Claims 5, 8-11, 13 and 20-25, as amended hereby, are

now directed to a cell or transgenic mouse having a stefin homolog gene identified as SEQ ID NO: 1 that has been disrupted by homologous recombination and which cell (when used to produce a transgenic mouse) or transgenic mouse, when homozygous for the disruption, exhibits an increased activity phenotype or a neuropsychological disorder phenotype. As such, the Applicants submit that the rejections are overcome by this amendment and respectfully request that these rejections be withdrawn.

Claims 5, 6 and 13 have been asserted to be non-enabling “for any cell other than a cell derived from the transgenic mouse or a mouse ES cell.” (Office Action dated January 14, 2003, page 4) The Office Action also asserted that “the disclosure is enabling only for a cell derived from a KO mouse . . . [and] for an ES cell.” Claims 5, 6 and 13, as amended hereby, specifically recite a “murine embryonic stem cell.” Thus, the Applicants submit that the rejections are overcome by this amendment and respectfully request that these rejections be withdrawn.

Claims 11 and 13 have also been asserted to be non-enabling for “a method by which expression of a gene that has been disrupted can be measured.” (Office Action dated January 14, 2003, page 5) The Office Action also asserted that “the specification is enabling for ‘a method of identifying an agent that modulates the expression and/or function of a stefin [homolog gene] and thereby ameliorates a phenotype associated with the disruption.’” Claims 11 and 13 encompass the phenotypes of stem cells and/or transgenic mouse of claims 5 and 8. The Applicants have amended claims 11 and 13 to be drawn to a method for identifying an agent that ameliorates the encompassed phenotypes. As such, the Applicants submit that the rejections are overcome by this amendment and respectfully request that these rejections be withdrawn.

Claim 10 has been rejected for assertedly being non-enabling because “neither the instant disclosure nor the prior art provide enablement for a method of producing a transgenic mouse from any cell other than a mouse ES cell.” (Office Action dated January 14, 2003, page 5) The Applicants have amended claim 10 to be drawn to homologous recombination using a murine embryonic stem cell. As such, the Applicants submit that the rejections are overcome by this amendment and respectfully request that these rejections be withdrawn.

Therefore, Applicants submit that the rejection of the above-cited claims under 35 U.S.C. § 112, first paragraph, is overcome in view of the amendments and remarks set forth herein. The Examiner is thus respectfully requested to withdraw this rejection.

**Rejection under 35 U.S.C. § 112, 1<sup>st</sup> paragraph (possession).**

Claims 1-11, 13, 18-26 and 28-32 have been rejected under 35 U.S.C. § 112, first paragraph, for assertedly not being adequately described in the disclosure. Claims 6-7, 12, 14-19 and 26-32 are canceled.

The Office Action asserts that targeting constructs “comprising all or a portion of the sequence set forth in SEQ ID NO: 1, methods of using said targeting constructs comprising all or a portion of the sequence set forth as SEQ ID NO: 1 and mice and cells comprising a disruption of the stefin homolog gene comprising the sequence set forth as SEQ ID NO: 1 meet the written description provision of 35 U.S.C. § 112, first paragraph.” (Office Action dated January 14, 2003, page 6) Applicants submit that the rejections are overcome by this amendment and respectfully request that these rejections be withdrawn.

Therefore, Applicants submit that the rejection of the above-cited claims under 35 U.S.C. § 112, first paragraph, is overcome in view of the amendments and remarks set forth herein. The Examiner is thus respectfully requested to withdraw this rejection.

**Rejection under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph.**

Claims 1-4 and 9-13 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The Office Action asserts that claim 9 is indefinite for being directed to a non-human transgenic animal because no antecedent basis in claim 8 for any transgenic animal other than a mouse is allegedly described. The Office Action suggests that “amending the claim such that it is directed to a cell derived from the transgenic mouse of claim 8 would overcome this rejection.” The Applicants have adopted this suggestion.

Therefore, Applicants submit that the rejection of the above-cited claims under 35 U.S.C. § 112, second paragraph, is overcome in view of the amendments and remarks set forth herein. The Examiner is thus respectfully requested to withdraw this rejection.

**Conclusion.**

Applicants submit that all of the pending claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-1271.

Respectfully submitted,  
DELTAGEN, INC.

Date: \_\_\_\_\_

By: \_\_\_\_\_

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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

1. (Twice Amended) A targeting construct [capable of homologous recombination with SEQ ID NO: 1], comprising:
  - (a) a first polynucleotide sequence homologous to at least a first portion of an endogenous murine stefin homolog gene comprising SEQ ID NO: 1;
  - (b) a second polynucleotide sequence homologous to [the] at least a second portion of the stefin homolog gene; [and]
  - (c) a selectable marker located between the first and second polynucleotide sequences; and
  - (d) wherein where said targeting construct is introduced into a murine embryonic stem cell and homologously recombines with the stefin homolog gene, said homologous recombination disrupts the stefin homolog gene.
2. The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.
3. (Twice Amended) A method of producing a targeting construct [capable of homologous recombination with SEQ ID NO: 1], the method comprising:
  - (a) providing a first polynucleotide sequence homologous to at least a first portion of an endogenous murine stefin homolog gene comprising SEQ ID NO: 1;
  - (b) providing a second polynucleotide sequence homologous to [the] at least a second portion of the stefin homolog gene;
  - (c) providing a selectable marker located between the first and second polynucleotide sequences; and
  - (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
4. (Twice Amended) A method of producing a targeting construct [capable of homologous recombination with SEQ ID NO: 1], the method comprising:
  - (a) providing a polynucleotide comprising a first sequence homologous to a first region of an endogenous murine stefin homolog gene comprising SEQ

ID NO: 1 and a second sequence homologous to a second region of [a] the stefin homolog gene; [and]

- (b) inserting a positive selection marker between the first and second sequences to form the targeting construct; and
- (c) wherein where said targeting construct is introduced into a murine embryonic stem cell and homologously recombines with the stefin homolog gene, said homologous recombination disrupts the stefin homolog gene.

5. (Twice Amended) A murine embryonic stem cell comprising a genome comprising a disruption in an endogenous stefin homolog gene comprising SEQ ID NO: 1; wherein said cell, when introduced into a blastocyst produces a transgenic mouse comprising a genome having a disruption in the stefin homolog gene, wherein where the mouse is homozygous for the disruption, the mouse exhibits, relative to a wild-type mouse, a phenotype selected from the group consisting of increased activity and a neuropsychological disorder [target gene sequence disrupted by homologous recombination of the target gene sequence with a sequence homologous to a region of SEQ ID NO: 1].

Claim 6 is canceled.

Claim 7 is canceled.

8. (Twice Amended) A transgenic mouse comprising a genome comprising a disruption in an endogenous stefin homolog gene comprising SEQ ID NO: 1; wherein where the disruption is homozygous, the transgenic mouse exhibits, relative to a wild-type mouse, a phenotype selected from the group consisting of increased activity and a neuropsychological disorder [target gene sequence disrupted by homologous recombination of the target gene sequence with a sequence homologous to a region of SEQ ID NO: 1].

9. (Amended) A cell derived from the [non-human] transgenic mouse [animal] of claim 8.

10. (Twice Amended) A method of producing a transgenic mouse comprising a genome comprising a disruption in an endogenous stefin homolog gene comprising SEQ ID NO: 1 [target gene sequence disrupted by homologous recombination of

the target gene sequence with a sequence homologous to a region of SEQ ID NO: 1], the method comprising:

- (a) introducing the targeting construct of claim 1 into a murine embryonic stem cell;
- (b) introducing the cell into a blastocyst;
- (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
- (d) breeding the chimeric mouse to produce the transgenic mouse.

11. (Twice Amended) A method of identifying an agent that ameliorates a phenotype associated with a disruption in a stefin homolog gene [modulates the expression of a stefin homolog], the method comprising:

- (a) providing the transgenic mouse of claim 8 ;
- (b) administering an agent to the [non-human transgenic animal] mouse; and
- (c) determining whether the [expression] phenotype [of stefin homolog in the mouse] is ameliorated [modulated].

Claim 12 has been canceled.

13. (Twice Amended) A method of identifying an agent that ameliorates a phenotype associated with a disruption in a stefin homolog gene [modulates the expression of stefin homolog], the method comprising:

- (a) providing the cell of claim 5;
- (b) contacting the cell with an agent; and
- (c) determining whether [expression of] the phenotype [stefin homolog is modulated], produced by the insertion of the cell into the blastocyst according to claim 5, is ameliorated.

Claim 14 has been canceled.

Claim 15 has been canceled.

Claim 16 has been canceled.

Claim 17 has been canceled.

Claim 18 has been canceled.

Claim 19 has been canceled.

20. (Amended) The transgenic mouse of claim [1]8, wherein the increased activity is characterized by increased velocity of movement in an open-field test[, relative to a wild-type mouse].
21. (Amended) The transgenic mouse of claim 8, wherein the neuropsychological disorder comprises a [transgenic mouse exhibits] decreased propensity for despair or depression[, relative to a wild-type mouse].
22. (Amended) The transgenic mouse of claim 21, wherein the decreased propensity for despair or depression is characterized by a decreased amount of time spent immobile when tail-suspended [time in a tail suspension test, relative to a wild-type mouse].
23. (Amended) The transgenic mouse of claim 8, wherein the neuropsychological disorder comprises [transgenic mouse exhibits] a stimulus-processing deficit [relative to a wild-type mouse].
24. (Amended) The transgenic mouse of claim [18] 23, wherein the stimulus-processing deficit is characterized by decreased pre-pulse inhibition.
25. (Amended) The transgenic mouse of claim [8] 24, wherein the decreased pre-pulse inhibition is consistent with [transgenic mouse exhibits] schizophrenic behavior.

Claim 26 has been canceled.

Claim 27 has been canceled.

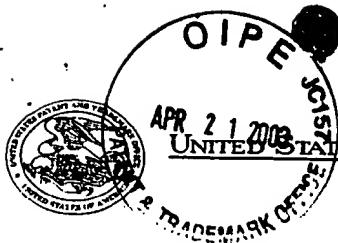
Claim 28 has been canceled.

Claim 29 has been canceled.

Claim 30 has been canceled.

Claim 31 has been canceled.

Claim 32 has been canceled.



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,180	07/11/2001	Keith D. Allen	R-477	1187

7590 01/14/2003

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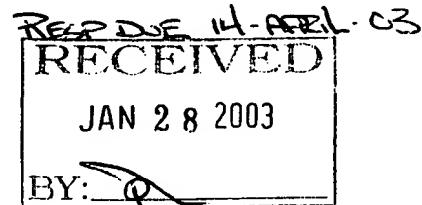
EXAMINER

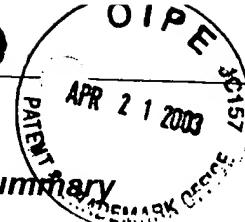
SULLIVAN, DANIEL M

ART UNIT	PAPER NUMBER
1636	15

DATE MAILED: 01/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.





## Office Action Summary

Application No.	Applicant(s)	
09/904,180	ALLEN, KEITH D.	
Examiner	Art Unit	
Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

1) Responsive to communication(s) filed on 31 October 2002.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

4) Claim(s) 1-11, 13, 16 and 18-32 is/are pending in the application.

4a) Of the above claim(s) 16 and 27 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-11, 13, 18-26 and 28-32 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on 28 October 2002 is/are: a) accepted or b) objected to by the Examiner. Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner. If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some \* c) None of:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 14.

4) Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.

5) Notice of Informal Patent Application (PTO-152)

6) Other: \_\_\_\_\_

### **DETAILED ACTION**

This Office Action is a response to the "Amendment Under 37 C.F.R. §1.111" filed October 31, 2002(Paper No. 13) in reply to the Office Action mailed June 19, 2002 (Paper No. 11). Claims 1, 3-5, 8, 10, 11, 13, 18, 21, 23, 25 and 26 were amended, claims 12, 14, 15 and 17 were canceled and claims 28-32 were added in Paper No. 13. Claims 16 and 27 were withdrawn from consideration in Paper No. 11. Therefore, claims 1-11, 13, 18-26 and 28-32 are pending and under consideration in the application.

#### *Election/Restrictions*

This application contains claims 16 and 27 drawn to an invention nonelected with traverse in Paper No. 10. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

#### *Drawings*

The corrected or substitute drawings were received on October 28, 2002. These drawings are acceptable.

#### *Response to Amendment*

All rejections as they pertain to claims 12, 14, 15 and 17 are rendered moot by the cancellation of those claims in Paper No. 13.

Applicant has not supplied a clean copy of claim 11. Applicant must supply a clean copy of claim 11 with the response to this Office Action.

***Claim Rejections - 35 USC § 112, first paragraph (enablement)***

Claims 5-11, 13 and 18-26 stand rejected, and new claims 28-32 are rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement for the full scope of the claims for the reasons set forth in Paper No. 11.

In response to the rejection, applicant has amended claims 5, 8 and 10 such that they are now directed to cells and mice, and methods of producing cells and mice, comprising a “genome comprising a target sequence disrupted by homologous recombination...with a sequence homologous to a region of SEQ ID NO:1”. Applicant argues, “the amended claims are not concerned, as the Examiner asserts...with ‘any disruption in any stefin homologue gene’” (Paper No. 13, page 5). However, the amendment is not sufficient to overcome the rejection because the claims still encompass subject matter beyond what is enabled by the disclosure. As stated in the previous Office Action, “the specification is enabling for a homozygous knockout mouse comprising a disruption in the stefin homologue gene set forth in SEQ ID NO:1 and exhibiting phenotypic features such as hyperactivity, decreased propensity to despair, schizophrenic behavior and decreased prepulse inhibition as compared to wild-type mice” (Paper No. 11, page 3). The amended claims, and the claims added in Paper No. 13, encompass products and methods comprising disruption of *any* gene that is homologous to a sequence that is homologous to a region of SEQ ID NO:1. In other words, the disrupted gene need not comprise the sequence set forth as SEQ ID NO:1, it need only be sufficiently homologous to a sequence that has some unspecified degree of homology to SEQ ID NO:1 for recombination to occur. Furthermore, the cells and animals of claims 5-9 and 28-32 need not comprise a disruption that results in a

phenotype that is enabled by the teachings of the specification. The Office Action clearly states that the disclosure is only enabling for disruption of a target gene comprising the sequence set forth in SEQ ID NO:1, wherein an animal that is homozygous for the disruption expresses a phenotype including hyperactivity, decreased propensity to despair, schizophrenic behavior and decreased prepulse inhibition as compared to wild-type mice.

Furthermore, claims 5, 6 and 13 still encompass a cell, and method of using said cell, other than an embryonic stem cell or cell derived from a transgenic animal. The previous office action clearly states that the disclosure is enabling only for a cell derived from a KO mouse (final sentence on page 3). In addition to a cell obtained from the knockout mouse, the disclosure is enabling for an ES cell comprising disruption of the stefin homologue gene comprising the sequence set forth as SEQ ID NO:1, which can be used to make a knockout mouse that, when homozygous for the disruption, expresses a phenotype including hyperactivity, decreased propensity to despair, schizophrenic behavior and decreased prepulse inhibition as compared to wild-type mice. For reasons of record in Paper No. 11, the disclosure is not enabling for any cell other than a cell derived from the transgenic mouse or a mouse ES cell.

Claims 11 and 13 also stand rejected for being directed to a method of identifying an agent that modulates the expression of a stefin homologue in an animal comprising a disruption in the stefin homologue gene by any means other than amelioration of a phenotype associated with homozygous disruption of the stefin homologue gene comprising the sequence set forth as SEQ ID NO:1. As stated in the previous office action, the specification is enabling for "a method of identifying an agent that modulates the expression and/or function of a stefin protease inhibitor gene and *thereby ameliorates a phenotype associated with the disruption*" (page 10,

first full paragraph). The specification does not teach a method by which expression of a gene that has been disrupted can be measured; therefore, for reasons of record in Paper No. 11, claims 11 and 13 stand rejected under 35 U.S.C. § 112, first paragraph.

Finally, claim 10 stands rejected in being directed to a method of producing a transgenic mouse, which comprises in step (a) introducing a targeting construct into any cell other than a mouse embryonic stem cell. As stated in the first full paragraph on page 9 of the previous office action, “[s]ince homologous recombination is required for gene targeting methods such as employed in the instant invention, embryonic stem (ES) cell technology must be available to carry out the method.” Neither the instant disclosure nor the prior art provide enablement for a method of producing a transgenic mouse from any cell other than a mouse ES cell.

***Claim Rejections - 35 USC § 112, first paragraph (possession)***

Claims 1-11, 13 and 18-26 stand rejected, and new claims 28-32 are rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description for the full scope of the claims for the reasons set forth in Paper No. 11.

In response to the rejection, applicant has amended claims 1, 3 and 4 such that they are now directed to a targeting construct “capable of homologous recombination with SEQ ID NO:1”, and claims 5, 8 and 10 such that they are now directed to cells and mice, and methods of producing cells and mice, comprising a “genome comprising a target sequence disrupted by homologous recombination...with a sequence homologous to a region of SEQ ID NO:1”. The amended claims are still directed to products and methods which require possession of a genus of stefin homologue genes which are not adequately described in the disclosure (i.e. any gene other

than the a gene comprising the sequence set forth as SEQ ID NO:1). Therefore, for reasons of record in Paper No. 11, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of genes comprising a sequence *homologous* to a region of SEQ ID NO:1. Therefore, only the described targeting constructs comprising all or a portion of the sequence set forth as SEQ ID NO:1, methods of using said targeting constructs comprising all or a portion of the sequence set forth as SEQ ID NO:1 and mice and cells comprising a disruption of the stefin gene comprising the sequence set forth as SEQ ID NO:1 meet the written description provision of 35 U.S.C. §112, first paragraph.

#### ***Claim Rejections - 35 USC § 103***

Rejection of claims 1-11, 13 and 18-26 under 35 U.S.C. § 103(a) as unpatentable over Tsui *et al.* and Pennachio *et al.* further in view of Capecchi *et al.* is withdrawn in view of the amendments to the claims and arguments of record in Paper No. 13.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 and 9-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is indefinite in being directed to a cell derived from a “non-human transgenic animal”. There is no antecedent basis in claim 8 for any transgenic animal other than a mouse. Amending the claim such that it is directed to a cell derived from the transgenic mouse of claim 8 would overcome this rejection.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-9105 for regular communications and 703-746-9105 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

dms  
January 10, 2003

*Anne-Marie Falk*  
ANNE-MARIE FALK, PH.D  
PRIMARY EXAMINER